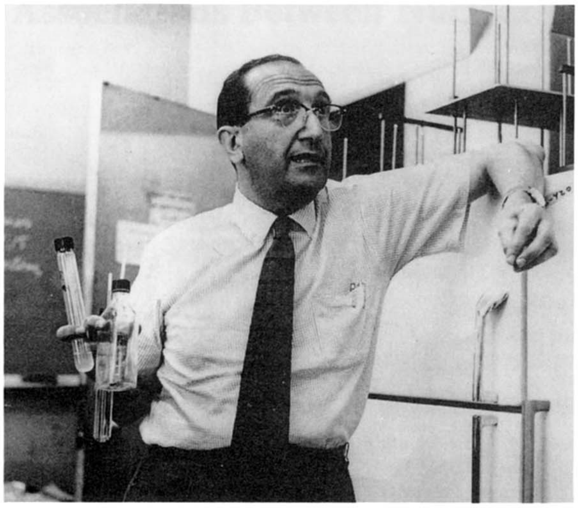

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# Salvador Edward Luria (1912–1991)

SALVADOR E. LURIA (SALVA to family and friends) died on the 6th of February, 1991 at his home in Lexington, Massachusetts. He was one of the protagonists who, in the early 1940s, brought bacteriophage into the limelight of genetics and helped to develop this area of research into one of the roots of molecular biology as we know it today. This was recognized in 1969 with a Nobel Prize shared with MAX DELBRÜCK and ALFRED D. HERSHEY.

He was born SALVATORE LURIA in Turin, Italy, of a Jewish family, and attended medical school there, frequenting the histology laboratory of professor GIUSEPPE LEVI[1] as an intern. While specializing in radiology at Turin and, later, serving in the Italian army as a medical officer, LURIA began to consider a career in basic science as a more appealing alternative to medicine. UGO FANO[2] was instrumental in this reappraisal. LURIA started to study calculus and physics and, in the fall of 1937, having moved to Rome to complete his specialization in radiology, was admitted as some kind of lowly trainee in ENRICO FERMI's extended group at the Physics Institute[3] of the University of Rome. Here FRANCO RASETTI[4] called LURIA's attention to the radiogenetic work on Drosophila[5] by H. J. MULLER and by N. W. TIMOFÉEF-RESSOVSKY, and particularly to DELBRÜCK's examination of the concept of the gene in physical terms.[6] Also in Rome, LURIA met GEO RITA,[7] a microbiologist, and was introduced by him to bacteriophage. LURIA was intrigued at the possibilities of bacteriophage for radiobiological work and started a series of experiments with RITA's help.[8] His resolve was further strengthened by learning (presumably through RASETTI) that DELBRÜCK, who was by then in the United States, had also started working on bacteriophage.

Sadly, the Rome period was short lived. In July, 1938 the Fascist regime proclaimed the "racial manifesto." Jews were thrown out of jobs. Many emigrated. LURIA had been awarded an Italian fellowship for study in the United States but it was suddenly with-

[1] GIUSEPPE LEVI (1872–1965), professor of human anatomy and one of the earliest tissue culture experts, had a large following of research students, two other Nobel prize winners (RENATO DULBECCO and RITA LEVI-MONTALCINI) among them. A socialist, he was openly opposed to the Fascist regime, was briefly jailed, and spent some time in hiding during the war. His strong and colorful personality emerges in N. GINZBURG's *Family Sayings* (translated by D. M. LOW from *Lessico Famigliare*; E. P. Dutton, New York, 1967) and *passim* in C. BARIGOZZI's *La Stanza di Genetica* (Francesco Nastro, Luino, 1981), R. DULBECCO's *Scienza, Vita e Avventura* (Sperling & Kupfer, Milan, 1989), R. LEVI-MONTALCINI's *In Praise of Imperfection: My Life and Work* (Basic Books Publishers, New York, 1988), and LURIA (1984).

[2] UGO FANO (b. 1912), later professor of physics at the University of Chicago, was a high school friend of LURIA's. He emigrated to the United States in 1938 and collaborated with M. DEMEREC in the early 1940s at Cold Spring Harbor on radiation-induced mutations in Drosophila.

[3] The Department of Physics at the University of Rome was then at the peak of its fame. Its director, O. M. CORBINO, eminent scientist, administrator and politician, had been able to obtain extensive support for ENRICO FERMI and his collaborators. CORBINO's sudden death in 1937 probably accelerated the diaspora of that group, already destabilized by the political situation (see Chapter 5 of G. HOLTON's *The Scientific Imagination: Case Studies*, Cambridge University Press, 1978). For a sensitive although historically not quite correct literary recreation of the mood in the physics group as the war approached, see L. SCIASCIA's *La Scomparsa di Majorana* (Einaudi, Turin, 1975; translated by S. RABINOVICH as *The Mystery of Majorana*, Carcanet Press, 1987).

[4] FRANCO RASETTI (b. 1901), close friend and colleague of FERMI, like him professor of physics at Rome, author of one of the earliest textbooks of nuclear physics. He left Europe for Canada in 1938 and joined Johns Hopkins University in 1947. His broad scientific interests included biology and paleontology. It seems likely that RASETTI and DELBRÜCK had known each other since the early 1930s. RASETTI spent part of 1931–1932 in LISE MEITNER's laboratory at Berlin-Dahlem, which DELBRÜCK joined in 1932.

[5] LURIA, with a medical school background, had apparently no direct connection with the few Italian geneticists of the time.

[6] This was part of a classic 1935 paper by N. W. TIMOFÉEF-RESSOVSKY, K. ZIMMER and M. DELBRUCK (*Nachr. Ges. Wiss. Göttingen* **1:** 189–245) "representing a cooperation between genetics and physics" (quoted from its preface), the impact of which is discussed at length by STENT (1982) and by E. P. FISCHER and C. LIPSON (in *Thinking about Science: Max Delbrück and the Origins of Molecular Biology*, W. W. Norton, New York, 1989). A shorter version of this paper was presented by TIMOFÉEF-RESSOVSKY at a conference in Paris in 1937. TIMOFÉEF-RESSOVSKY's laboratory in Berlin-Buch was a casualty of the war. He, a Soviet citizen, was taken to the Soviet Union where he lived on in rather sad circumstances and died in 1981. ZIMMER, the co-author of the 1935 paper, followed TIMOFÉEF-RESSOVSKY to the Soviet Union but later was able to return to West Germany to continue working in radiation biology at the Nuclear Research Center in Karlsruhe, near Heidelberg.

[7] GEO RITA (b. 1911), later professor of virology at the University of Rome, was working at the time on bacterial contamination of water and had isolated some phages in the course of this work.

[8] These experiments, probably planned in consultation with RASETTI (see L. FERMI's *Illustrious Immigrants: The Intellectual Migration from Europe 1930–1941*, University of Chicago Press, 1968), reexamined the question of whether a single bacteriophage particle was sufficient for infection in liquid culture. They were published the following year in France.

drawn. Instead, he was able to move to Paris, where FERNAND HOLWECK[9] obtained a stipend for him at the Radium Institute. They collaborated with EUGÈNE WOLLMAN[10] to measure the target size of a bacteriophage exposed to different kinds of ionizing radiations (WOLLMAN, HOLWECK and LURIA 1940).

But world events were pressing on. World War II started in September, 1939. By late Spring of 1940 the Germans were approaching Paris. LURIA left by bicycle. In Marseilles he succeeded in obtaining an American visa. He proceeded through Spain to Portugal, where in September he boarded the ship that took him to New York.[11]

In New York, with the help of FERMI (who had himself emigrated in 1938) and of LESLIE C. DUNN and the Rockefeller Foundation, LURIA was able within weeks to again pursue radiobiological work with bacteriophage (in collaboration with the physicist FRANK M. EXNER) at Columbia University. He also very soon sought contact with DELBRÜCK, then at Vanderbilt University. Their first meeting led to a collaboration, both by correspondence and through bouts of joint experimental work at Nashville and Cold Spring Harbor, that was to last for more than a decade.

In 1943 LURIA obtained a faculty position at Indiana University in Bloomington,[12] where he taught bacteriology and started a course in virology. There he met and married ZELLA HURWITZ, a psychologist and now professor at Tufts University. DANIEL, their only child and now an economist, was born in 1948. In 1950 LURIA moved to the University of Illinois in Urbana.[13] Nine years later he joined the Biology Department at the Massachusetts Institute of Technology, where he remained to the end of his days. For several years he also held administrative responsibilities as the first director of MIT's Center for Cancer Research. Both at Illinois and at MIT, LURIA had a lasting impact on their instructional and research programs.

LURIA's most influential research contributions preceded the "year of DNA" (1953). During this period he continued radiobiological studies of bacteriophage (target size determination, the "indirect effect" and "Luria-Latarjet curves") (LURIA and EXNER 1941; LURIA and LATARJET 1947), experimented with multiple and mixed infection as tools for probing the intracellular behavior of bacteriophage (DELBRÜCK and LURIA 1942; LURIA and DELBRÜCK 1942; LURIA 1947; LURIA and DULBECCO 1949), discovered mutational "jackpots" and invented the "fluctuation test" for spontaneous mutation (LURIA and DELBRÜCK 1943), was a key participant in the early electron microscopal studies of the shapes and sizes of bacteriophage particles (LURIA and ANDERSON 1942; LURIA, DELBRÜCK and ANDERSON 1943), examined a variety of bacterial and bacteriophage mutation types (LURIA 1945, 1946) with implications for the mechanism of phage reproduction based on the clone-size distributions of spontaneous mutants (LURIA, 1951), and recognized the first case of what we now call "restriction and modification" (LURIA and HUMAN 1952; LURIA 1953).

Although the concept of mutation was already being freely applied to bacteria and viruses by the few practitioners, the fluctuation test for spontaneous mutations established a new and rigorous criterion and a new technique for measuring mutation rates. Its mathematical subtleties kept biostatisticians busy for years afterward, while its technical simplicity obviated entanglements with the still extant experimental and semantic problem of how a mutation becomes established.

Restriction and modification was a different story. In this case the heightened confidence in the applicability of basic genetic principles to bacteria and viruses brought out the apparent absurdity of very simple, accidental observations and the recognition of a new, quite general phenomenon. It then took years of hard work in many laboratories to elucidate the diverse enzymatic processes that modify DNA.

The initial collaboration of DELBRÜCK and LURIA established the foundation for a research movement focused on bacteriophage, a movement that grew beyond all expectations and recruited not only their graduate students and close collaborators but also attracted scientists from a variety of fields. It later merged with molecular biology. Much has been written about the "phage group" and this larger research movement (*e.g.*, CAIRNS, STENT and WATSON 1966) and need not be repeated here.[14] In fact, the attraction of bacteriophage as experimental material remained

[9] FERNAND HOLWECK (1890–1941), well known French radiation physicist, was later arrested by the German occupation troops and died in jail.

[10] EUGÈNE WOLLMAN (1883–1943?) was then the leading bacteriophage specialist at the Institut Pasteur. He was engaged at the time in comparing bacteriophage radiobiological target sizes with size determinations from ultrafiltration. He had earlier speculated about the possibility of a biological relationship between bacteriophage and genetic material (see PH. HADLEY's 1926 review in *J. Infect. Dis.* **42:** 263–434). Both WOLLMAN and his wife, also a scientist, were deported by the Nazis in 1943 and disappeared at Auschwitz (see P. NICOLLE, 1946, *Ann. Inst. Pasteur* **72:** 855–858).

[11] I have told this part of LURIA's life in some detail, largely based on his autobiography (LURIA 1984), because it shows three historically interesting aspects of the beginnings of modern bacteriophage research: the troubled wartime background, the network of European emigrés and, above all, the "physics connection." See D. FLEMING's "Émigré physicists and the biological revolution" (in *The Intellectual Migration: Europe and America, 1930–1960*, edited by D. FLEMING and B. BAILYN, Harvard University Press, 1969) and L. FERMI's book cited in footnote 8.

[12] Indiana was rather strong in biology, with T. M. SONNEBORN, R. E. CLELAND and, from 1945, H. J. MULLER, not to mention A. C. KINSEY of wasps and sex fame. J. D. WATSON came to Indiana to study genetics and became LURIA's first graduate student.

[13] Bacteriology at Illinois was being rejuvenated by H. ORIN HALVORSON, and with I. C. GUNSALUS, SOL SPIEGELMAN and LURIA under the same roof, it made for a very lively department.

[14] In an otherwise controversial article, F. M. BURNET wrote in the January 1, 1966, issue of *The Lancet*, "Almost the whole of the modern structure has been built on the standard strain of *Escherichia coli* B and two phages T2 and T4 . . . For thirty years I have watched this structure develop around the central bacterium-phage theme, bringing in as needed contributions from the chemistry of the nucleic acids and proteins, from the genetics of higher organisms, and from the pharmacology of antibiotics. It has been a magnificent achievement, to be ranked with the elucidation of subatomic structure

unchallenged until powerful new biochemical techniques were developed which allowed effective manipulation of more complex organisms. As STENT (1982) correctly pointed out, the original innovations were in the first place methodological (rigor of inference, quantitation, use of genetic concepts, careful limitations in the choice of material, striving for fundamentals), for which DELBRÜCK more than LURIA was the responsible ideologue. LURIA's impact derived from his numerous experimental contributions, his extensive teaching, his willingness to give talks and write textbooks and reviews, the breadth of his interests in microbiology and biochemistry, and his extensive contacts with the large constituency of professional bacteriologists and virologists.

In the post-DNA era, LURIA's research activities consisted mostly of guiding or advising graduate students and postdoctoral fellows on a variety of topics and experimental materials, usually concerning bacteriophage behavior or effects. In the sixties his interest shifted to colicins. He was intrigued by the fact that a single colicin molecule, a protein, could kill a bacterial cell by suddenly and dramatically blocking a number of cell functions. With several collaborators he focused on this problem for more than a decade. In particular, they analyzed the impact of colicin adsorption on active transport across the cell membrane (see LURIA 1975a).[15]

LURIA was a fluent, prolific writer. In 1953 he published a textbook of virology that stressed general biological principles and emphasized bacteriophage as a model. The outlines of his biology lectures for undergraduates at MIT (LURIA 1975b) make wonderful reading across the whole range of cellular processes. More literary efforts were a popular science book (LURIA 1973) and "a confessional account of himself"[16] (LURIA 1984).

Throughout most of his life LURIA was politically engaged. He had strong sympathies for leftist movements and called himself a socialist.[17] He was basically a pacifist, more sensitive to inequalities of class and social injustice than to the deadening consequences of state socialism or the threat of world communism. He seems to have enjoyed the type of social intercourse that goes with political activism, and this fulfilled an emotional need more than it reflected a coherent philosophy.

as one of the two major triumphs of twentieth century experimental science." Although better known for his later work in immunology and on animal viruses, BURNET had done outstanding work on bacteriophages in the 1930s using both virulent and lysogenic systems. Phage C16, used by WOLLMAN, HOLWECK and LURIA (1940), had in fact been isolated by BURNET; it is a member of the same family as T2 and T4.

[15] This work prepared the way for the major 1978 finding of S. J. SCHEIN, B. L. KAGAN and A. FINKELSTEIN (*Nature* **276:** 159–163), who showed that a colicin could establish a nonselective, ion-permeable channel in bilayer membranes, leading to the collapse of the membrane proton motive force.

[16] The quote is from the 1984 book review by S. BRENNER (*Nature* **308:** 794).

[17] Because of his politics, LURIA was for several years unable to travel abroad and was blacklisted by the National Institutes of Health.

I was with LURIA for almost five years as a research associate, initially at Bloomington and then at Urbana. His work at that time was still centered on the growth cycle of bacteriophage T2. Even though he was at first hesitant about my starting a new project, on lysogeny, he obtained the needed strains for me and supported my work in every possible way. Especially at Urbana, he already was heavily engaged in teaching, writing and guiding graduate students. He worked on a regular schedule, always with intensity. He had a great capacity for taking in information, scanning papers and books. A fluent verbalizer, he often gave the impression of building ideas as he was talking. He was always concerned about the welfare of students and coworkers, yet he suffered alternating moods and could be aggressive and irritable at some times while buoyant, even whimsical, at others. I remember the reaction of the late PAT MCGRADY, science editor for the American Cancer Society, after a long conversation with LURIA. MCGRADY had visited our laboratory to gather material for an article on the phage work. While I accompanied him out of the building, he checked with me some of the things he had learned from LURIA. As we were parting he paused a moment and then said, almost to himself, "He is so human!"

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